



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of	)	<b>MAIL STOP AF</b>
Masayuki Furuya et al.	)	
Application No.: 10/518,640	)	Group Art Unit: 1623
Filing Date: December 20, 2004	)	Examiner: Ganapathy Krishnan
Title: PROCESS FOR PRODUCING	)	Confirmation No.: 2846
GLYCOSIDE	)	

**PRE-APPEAL BRIEF REQUEST FOR REVIEW**

Commissioner for Patents  
P.O. Box 1450  
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Sir:

Applicants request a Pre-Appeal Brief Conference to seek further review of the above-identified application. No amendments are being filed with this Request. A Notice of Appeal is being concurrently filed with this Request.

For at least the following reasons, the rejection of claims 1 and 21-23 under 35 U.S.C. §103(a) as being obvious over Japanese Patent Document No. 62-263194 (*JP '194*), Japanese Patent Document No. 2000-319116 (*JP '116*) and "Introduction to General, Organic & Biochemistry" (*Bettelheim et al*), set forth in the final Official Action dated March 10, 2009, are clearly improper and without basis.

1. Glycoside represented by formula (3)

Independent claim 1 recites a method for preparing a glycoside represented by formula (3), wherein any one of R2, R3 and R4 represents a hydroxyl, and each of the remaining two of R2, R3, and R4 represent a residue formed by reacting glucose pentaacetate with a hydroxyl

group of an alkyl gallate. Thus, the recited glycoside comprises **at least two residues** formed by reacting glucose pentaacetate with a hydroxyl group of an alkyl gallate.

None of the excerpts of *JP '194* cited at page 3 of the final Official Action discloses or suggests a glycoside comprising at least two residues formed by reacting glucose pentaacetate with a hydroxyl group of an alkyl gallate, as is presently claimed. By comparison, *JP '194* is concerned with the preparation of a tetraacetyl arbutin, and provides no indication of the desirability for preparing a glycoside comprising at least two residues formed by reacting glucose pentaacetate with a hydroxyl group of an alkyl gallate. This deficiency is discussed at pages 4-6 of the Amendment and Reply filed on September 10, 2008.

The secondary applied documents (i.e., *JP '116* and *Bettelheim et al*) fail to cure such deficiencies of *JP '194*. The Examiner has relied on *JP '116* for disclosing the use of boron trifluoride etherate. See final Official Action at page 4. The Examiner has relied on *Bettelheim et al* for disclosing a reaction between a carboxylic acid and a phenolic hydroxyl in the presence of acid catalyst to give a corresponding ester. See final Official Action at page 4.

As noted above, *JP '194* is not concerned with the preparation of a glycoside comprising at least two residues formed by reacting glucose pentaacetate with a hydroxyl group of an alkyl gallate. Rather, *JP '194* relates to a process for preparing a tetraacetyl arbutin product. There is no indication of the desirability of preparing the claimed glycoside in the production of the *JP '194* tetraacetyl arbutin product. Thus, even in view of the secondary applied documents, it would not have been obvious to modify *JP '194* to result in the preparation of a glycoside comprising at least two residues formed by reacting glucose pentaacetate with a hydroxyl group of an alkyl gallate.

Further, like *JP '194*, the secondary applied documents do not disclose or suggest a method for preparing a glycoside comprising at least two residues formed by reacting glucose pentaacetate with a hydroxyl group of an alkyl gallate, as is presently claimed

2. Reaction temperature

*JP '194* does not disclose or suggest reacting an alkyl gallate having a C<sub>1</sub>-C<sub>10</sub> straight or branched alkyl with glucose pentaacetate in the presence of an organic solvent and an acid catalyst at 30°C to 60°C, as recited in claim 1. This deficiency of *JP '194* is discussed at pages 4-6 of the Amendment and Reply filed on September 10, 2008. By comparison, *JP '194* discloses a reaction temperature range of around 90-120°C, under a pressure of 3 -150 mmHg.

Comparative Experiment 2 of the Declaration Under 37 C.F.R. §1.132 of Akinori Nagatomo executed on July 7, 2008 (hereinafter "Declaration"), shows, for example, the significance of the reaction temperature in a method for preparing a glycoside comprising at least two residues formed by reacting glucose pentaacetate with a hydroxyl group of an alkyl gallate. In this regard, Comparative Experiment 2 differs from the claimed method in that a reaction temperature of 80°C was employed, which is outside the scope of the claimed temperature range of 30°C to 60°C. In Comparative Experiment 2, the reaction did not proceed at six hours after starting the reaction, and the reaction was stopped at eight hours after starting the reaction. Such experiment taken in connection with the other experiments set forth in the Declaration, show the significance of the claimed reaction temperature range in the preparation of a glycoside comprising at least two residues formed by reacting glucose pentaacetate with a hydroxyl group of an alkyl gallate. The applied art has no recognition of such result-effective relationship between the reaction temperature and the preparation of a glycoside comprising at least two residues formed by reacting glucose pentaacetate with a hydroxyl group of an alkyl gallate. Thus, it would not have been obvious to modify *JP '194* to arrive at the claimed reaction temperature of 30°C to 60°C.

3. Acetic acid concentration in the reaction system

*JP '194*, *JP '116* and *Bettelheim et al* do not disclose or suggest maintaining the concentration of the acetic acid in the reaction system at 1.0 percent by weight or less during the

reaction, as recited in claim 1. The Examiner has taken the position that it would have been obvious to modify *JP '194* to arrive at maintaining such acetic acid concentration in view of *Bettelheim et al*, which allegedly teaches that the presence of acetic acid leads to "a side reaction that would prevent the formation of the diglycoside." Final Official Action at page 4. However, *JP '194* is not concerned with the preparation of a diglycoside; there is no indication of the desirability of preparing a diglycoside in the production of *JP '194*'s tetraacetyl arbutin product. As such, it would not have been obvious to modify *JP '194* by maintaining the concentration of the acetic acid in the reaction system at 1.0 percent by weight or less during the reaction. This deficiency of *JP '194* is discussed at pages 4-6 of the Amendment and Reply filed on September 10, 2008.

Claim 1 also recites removing from the reaction system organic solvent and acetic acid formed during the reaction, wherein a distillate comprising said acetic acid and organic solvent both removed from the reaction system is distilled off at a rate of 20 to 500 g/hr relative to one mol of the alkyl gallate having C<sub>1</sub>-C<sub>10</sub> straight or branched alkyl. Applicants submit that the recited removal rate can be effective, for example, to maintain the claimed acetic acid concentration in the reaction system. This can in turn, lead to a relatively higher yield of glycoside comprising at least two residues formed by reacting glucose pentaacetate with a hydroxyl group of an alkyl gallate. See, for example, Example 1 and Comparative Example 2 of the present specification. By comparison, and as discussed above, *JP '194* is not concerned at all with the preparation of a glycoside comprising at least two residues formed by reacting glucose pentaacetate with a hydroxyl group of an alkyl gallate. As such, it would not have been obvious to modify the *JP '194* process to arrive at the claimed removal rate.

#### 4. Unexpected results

The Declaration Under 37 C.F.R. §1.132 of Akinori Nagatomo executed on July 7, 2008, shows surprising and unexpected results attainable by employing exemplary methods for

preparing a glycoside, for example, when the temperature range, acetic acid concentration and removal rate specified in the claims are employed. In the Declaration, Experiments 1 and 4 correspond to Examples 1 and 6, respectively, in the present specification. Further, Experiment 5 in the Declaration corresponds to Example 1 described in *JP '194*. As can be seen from the results, in Experiment 5, high yields of a mono-glycoside were obtained. In contrast, in Experiment 4 of the Declaration, the method recited in the present claims is used to prepare a hydroquinone derivative. The results of Experiment 4 demonstrate that the exemplary method produces high yields of a diglycoside, and extremely low yields of mono-glycoside were obtained as compared to those of the diglycoside. The experimental data shows the surprising and unexpected results attainable when employing the claimed temperature range, acetic acid concentration and removal rate specified in the claims, in the preparation of a glycoside comprising at least two residues formed by reacting glucose pentaacetate with a hydroxyl group of an alkyl gallate. Such experiments are discussed in greater detail at pages 4-6 of the Amendment and Reply filed on September 10, 2008.

The Examiner has not established that independent claim 1 of the present application is rendered obvious over the applied art. Therefore, such claim, along with all claims which depend therefrom, are allowable.

No fee is believed to be due in connection with the filing of this paper. However, the Director is hereby authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY PC

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